

## RE: RfD data Fitting Results to date

Brattin, Bill to: Benson.Bob

09/15/2010 07:50 AM

From: "Brattin, Bill" <brattin@srcinc.com>

To:

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I doubt the latency time will be for a full lifetime. I suspect it will increase to some value, the level off and show no further increase. Can this be built into the lag time? However, what would be the effect of continued exposure on latency?

Latency (L) is the time between first exposure and the time you wish to determine if an adverse effect has occurred.? Consider some individual who is exposed to concentration C for duration d years beginning at age a.? The risk model will calculate the probability p that individual will develop disease from cumulative exposure  $C*d$  at some age  $a + L$ .? Assuming that risk (p) increases as a function of L (this seems very clear), then p will increase as long as L is increasing (i.e., as the person is getting older).? **In other words, the RfC depends on the age at first exposure, rather than being a constant.**? This is the same approach that has been used for cancer: there is not one unit risk, but a big table of values that depend on age at first exposure and duration of exposure.? **We could do the same thing for non-cancer.**? I think this would be much better than having a single value.

If you don't have a table of multiple values, then you have to specify the latency.? Because the risk will be highest for an individual who is exposed early in life, I think you would have to specify  $L = 70$ .? This will yield the right estimate for developing disease by age 70 in an individual who is first exposed at birth, but will strongly over-estimate risks for people who are not exposed until later in life.

The use of a lag period (e.g., 5 years) simply ignores the effect of exposure that has occurred within the most recent 5 years of life.? For example, if a person were exposed to 1 f/cc from age 20 to 22, the cumulative exposure (CE) and CE10 (CE lagged by 10 years) would be:

Age???? CE????? CE10

20????? 1??????? 0

21????? 2??????? 0

22????? 3??????? 0

24????? 3??????? 0

25????? 3??????? 1

26????? 3??????? 2

27????? 3??????? 3

28????? 3??????? 3

etc

This lag is important when fitting the data if the latency tends to be short.? In this case, most latency is long, so  $CE = CE10$  in nearly every case.? Still, I think it will be good to build a lag time into the model.

I need a calculation of the POD from the previous logistic regression (see the copy of appendix B from Monday) done taking into account both CE and age. Use the estimates from Model 2. Age can be 70 years. I think the confidence limits on the slope terms can be calculated using the  $1.645*SE$  (assuming the HQ people were correct about this).

I performed the calculation as you requested, and the result is 3.23 f/cc-yrs.? However, I do not think this value has any meaning.? First, the fitting used age rather than latency.? Second,

I think it is **very** simplistic to simply increase the slope by  $1.645 \times \text{stdev}$  without adjusting the other 2 parameters.? I am not sure exactly the best way to do this, but I am pretty sure the approach above is not optimal.

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**From:** Benson.Bob@epamail.epa.gov [mailto:Benson.Bob@epamail.epa.gov]

**Sent:** Tuesday, September 14, 2010 7:25 PM

**To:** Brattin, Bill

**Subject:** RE: RfD data Fitting Results to date

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